Response to Letter Regarding Article,  
“Intracoronary Injection of Large Stem Cells: Size Matters”

I thank Drs Gallet and Marbán1 for their interests in my editorial.2 I acknowledge that there are small reserved capillaries in the myocardium that may play a role in accommodating stem cells injected into the coronary artery. In my own experience in preclinical models, adenosine-induced maximal coronary flow reserve is 2 to 3 times from baseline measurements in the nonischemic myocardium.3 It is important to note, however, that even if the injection of cardiospheres opens up the reserved capillaries and some of cardiospheres do shift to these capillaries, the fate of the cells is not different and they will end up in 1 of the 4 destinations described in the editorial.2

In addition, we do not know how large the reserved capillaries are. Considering that they are closed in the normal state, it is likely that these newly recruited capillaries are smaller than normally perfused capillaries. Therefore, cardiospheres may be trapped more proximal to the branching of these smaller reserved capillaries and 1 clump of cardiospheres can possibly close several reserved capillaries. Thus, the actual reserve of the coronary capillaries for large stem cells can be much less than maximal coronary flow reserve.

Gallet and Marbán mention that cardiospheres transmigrate 24 to 72 hours after the intracoronary infusion. Although the permanent occlusion of the capillaries might be avoided through this mechanism, it does not prevent the acute occlusions after intracoronary infusion. Because the myocardium cannot survive 24 to 72 hours of ischemia, transmigration of cardiospheres at this time point in unlikely to prevent acute microinfarctions.

As indicated in the “Guidelines for Translational Research in Heart Failure,”1 safety is as important as efficacy in translating novel therapeutic approaches into clinics. Elucidating the threshold dose for intracoronary cardiospheres and demonstrating the efficacy with a sufficient safety margin will thus increase the likelihood of successful clinical translation using this cell type.

Disclosures

None.

Kiyotake Ishikawa, MD
Department of Cardiology
Cardiovascular Research Center
Icahn School of Medicine at Mount Sinai
New York, NY

References

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Kiyotake Ishikawa

Circ Cardiovasc Interv. 2015;8:
doi: 10.1161/CIRCINTERVENTIONS.115.002855
Circulation: Cardiovascular Interventions is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 1941-7640. Online ISSN: 1941-7632

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